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Adrenal stereotactic body radiation therapy: effects of a full and empty stomach on radiation dose to organs at risk

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SUMMARY

Background: Stereotactic Body Radiation Therapy (SBRT) has been reported to be curative in the treatment of oligometastases to the adrenal glands. However, the adrenals are surrounded by radiation-sensitive organs. We performed an Organ at Risk (OAR) analysis for SBRT to the left adrenal gland based on gastric state.

Patients and Methods: Twenty random stomachs were divided into "empty" or "full" groups of 10 each based on size. The PTV dose was 54 Gy/6 fx and D 95 coverage of PTV (CTV) (the dose to 95% of the PTV volume).

Results: The gastric OAR dose in the empty group was significantly lower than the full group. The OAR dose to the left kidney in the empty group was significantly higher than in the full group.

Conclusion: The smaller the stomach size, the lower the dose to the stomach. It is therefore better to perform SBRT on patients with an empty stomach.

Key words: stereotactic body radiotherapy, adrenal tumour, organ at risk, stomach

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INTRODUCTION

Evidence of the effectiveness of Stereotactic Body Radiation Therapy (SBRT) has recently been published [1-2]. Moreover, it has been reported that curative treatment for oligometastatic cancer where the primary lesion is controlled improves the disease-free recurrence time and overall survival. The adrenal glands are often the site of a solitary thoracic, abdominal, or pelvic metastasis, especially from lung cancer [3-11].

There is also a form of adrenal recurrence after radical resection of the primary lesion. There are reports that there is an advantage to use SBRT when there is an adrenal metastasis at the time of lung or breast cancer diagnosis, or when an adrenal metastasis appears after the completion of primary tumour treatment.

However, the adrenal glands are surrounded by radiation-sensitive organs, such as the pancreas, kidneys, small intestine, biliary system, and stomach. Thus, treatment planning requires close regulation due to the dose limit to the OAR. Radiation therapy can be adjusted for gastric capacity and cholecystic capacity (both include dietary restrictions). Hence we performed an OAR (Intestine, Pancreas, Liver, Right kidney, and spinal cord) analysis of SBRT to the left adrenal gland based on gastric state (empty or full stomach) at the time of irradiation. We examined whether it was possible to reduce the dose to the OAR.

MATERIALS AND METHODS

Included patients had prostate cancer or uterine cancer with treatment planning CTs images from the diaphragm to the pelvis and no history of abdominal organ dysfunction (i.e. cirrhosis, pancreatitis, renal atrophy). Of the 20 stomachs, that met our inclusion criteria, we divided 10 into a median larger group (considered a full stomach) and the other 10 into a smaller group (considered an empty stomach).

Deep Inspiration Breath Hold (DIBH) technique was used with the Abches system [12]. Patients were immobilized using an alpha cradle in the supine position with both arms over their heads. The main component of Abches was set over the iliac crest with two fulcrums placed and marked at the patient's sternum and abdomen. The Abches system was made from resin without electronic parts; thus, they only had minimal influence on dose calculation.

The "empty group" was defined as the smaller stomach group (n=10), whereas the "full group" was the larger stomach group (n =10). All radiation plans were created with a 3D treatment planning system (Elekta's XiO® treatment planning system and focal contouring system, Hamburg, Germany). An Elekta Synergy linear accelerator with 6 MV photon energy was used.

Adrenal ground and OAR were outlined by an abdominal radiation oncologist and medical physicists created the beam plans and the same radiation oncologist evaluated them. The radiation therapist performing the contouring and the medical physicist performing the treatment plan were blinded to patient information. The CTV was equal to the GTV. A 3mm isotropic margin was used to obtain the corresponding PTV. The prescribed PTV dose was 54 Gy/6 fx and D 95 coverage of PTV (the dose to 95% of the PTV volume). OAR dose limits are shown in Table 1. The capacity of the stomach was measured for its effects on OAR. Treatment regimens were analysed with a dose volume histogram and a one-way analysis of variance PTV was performed. All data are presented as mean ± standard deviation. We defined $p<0.05$ as statistically significant. We used a two-sided Wilcoxon rank-sum/Mann-Whitney U test using the Excel statistical software package (Excel-statistics 2015; Social Survey Research Information Co., Ltd., Tokyo, Japan). The primary results (D/V parameters) should be reported with both measures of central tendency (mean) and spread (SD or 95% CI). The very small sample size would indicate that the spread of the measurements would have had to have been extremely small (SD<2) for the results to have been statistically significant. We should report of the full results, i.e., a table of the PTV and OAR sizes as well as dosimetric parameters of each individual patient, which would be beneficial in assessing the results.

However, the internal organs to OAR this time, there are several variations in the case, depending on the shape of the parenchymal organs (liver, pancreas, and kidney) and the distance to the stomach. The amount and spread of visceral fat also vary extensively. Therefore, we have omitted the SD to improve the readability.

This study is a retrospective cohort comparison study. Informed consent was waived, and an opt out was available on the hospital homepage.

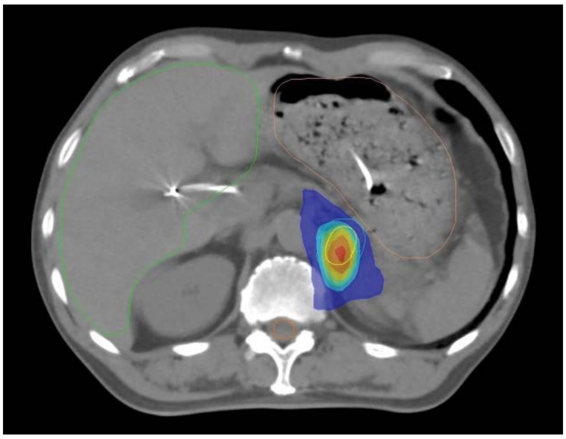

Fig.1. Adrenal SBRT administered in the setting of a large stomach

RESULTS

The stomach size of the empty group was 226 ± 98 cm^3, and the size of the full group was 480 ± 91 cm^3. A sample image of SBRT is shown in Figure 1. Interesting information can be observed in the tables. For example, readers want to know whether the stomach is empty do the other OARs receive higher dose (answer may be yes for left kidney).

An example of adrenal SBRT administered in the setting of a large stomach. The pancreas was not shown in this slice. CTV coverage is good. Yellow line: adrenal CTV (2 mm margin from GTV), OAR: Liver (green line), Stomach (orange line) (Figure 1).

The relationship between stomach size and OAR dose was measured. The gastric OAR dose in the empty group was significantly lower than in the full group (D5 and D10) (Tables 2 and 3). However, the OAR dose to the left kidney in the empty group was statistically significantly higher than in the full group (V12, V15, and V21). From table 2, it is evident that with an empty stomach, the left kidney receives significantly higher dose; this is of outmost importance because radiation oncologist must make a decision, i.e., should physician prefer stomach of kidney preservation. In this way, stomach seems to act as a natural spacer for abdominal organs.

An example of adrenal SBRT in the setting of a large stomach. The intestine is close to the left adrenal ground. CTV coverage is not good due to the intestine.

Tab. 1. Organ at risk (OAR) dose constraints applied for three fractions SBRT (54Gy/6fx for CTV) CTV is equal to PTV (Biological effective dose [BED10]) 102Gy Equivalent dose 2Gy (EQD) 85Gy. Radiation dose is limited to OAR

	D0.1 cc	D5.0 cc	D10.0 cc	V12 Gy	V15 Gy	V21 Gy
Stomach	≤ 22Gy		≤ 16Gy			
Intestine	≤ 22Gy	≤ 17 Gy	≤ 11Gy			
Pancreas	≤ 22Gy		≤ 12Gy	≤ 50%		≤ 30%
Liver					≤ 50%	≤ 30%
Kidneys (Left)				≤ 25%		
Kidneys (Right)				≤ 25%		
Kidneys (together)					≤ 35%	
Spinal cord	≤ 22Gy					

DX (the dose to X% of the OARs volume) at X values of 0.1, 5.0, and 10.0 cc. VX (the percentage of the OARs volume that received more than X Gy) CTV, clinical target volume; PTV, Planning target volume

Tab. 2. Dosing planned by medical physicist

		Empty	Full	p-value
PTV	D0.1 cc	65.8	66	0.31
	D5 cc	56.1	55.9	0.52
	D10 cc	42.4	43.1	0.47
	V12 Gy	99.9	99.9	0.5
	V15 Gy	99.6	99.8	0.22
	V21 Gy	96.8	99.8	0.38
Stomach	D0.1 cc	19.9	20.1	0.45
	D5 cc	13.7	15.9	0.03
	D10 cc	12.1	14.6	0.01
	V12 Gy	9.2	7.8	0.69
	V15 Gy	2.3	2.5	0.42
	V21 Gy	0	0	-
Intestine	D0.1 cc	17.8	15.3	0.2
	D5 cc	13.4	11	0.17
	D10 cc	12.2	9.6	0.15
	V12 Gy	4.2	5.1	0.6
	V15 Gy	1.3	2.1	0.66
	V21 Gy	0	0	-
Pancreas	D0.1 cc	45.6	38.9	0.23
	D5 cc	26.3	19.2	0.13
	D10 cc	20.5	13.6	0.09
	V12 Gy	73.4	48.4	0.06
	V15 Gy	60.9	39.5	0.08
	V21 Gy	37.9	22.2	0.08
Liver	D0.1 cc	15.4	13.6	0.24
	D5 cc	11.5	10.4	0.3
	D10 cc	10.4	9.3	0.29
	V12 Gy	2	0.8	0.12
	V15 Gy	0.5	0.1	0.14
	V21 Gy	0	0	-
Left kidney	D0.1 cc	50.3	50.7	0.53
	D5 cc	33.8	29.4	0.15
	D10 cc	25.2	20.8	0.12
	V12 Gy	23.8	15.6	0.01
	V15 Gy	19.1	12.9	0.01
	V21 Gy	12.6	8.4	0.03
Right Kidney	D0.1 cc	9.8	8.4	0.13
	D5 cc	6.9	5.9	0.21
	D10 cc	5.5	5.1	0.38
	V12 Gy	0.4	0	0.17
	V15 Gy	0	0	-
	V21 Gy	0	0	-
Spinal cord	D0.1 cc	14	14	0.5
	D5 cc	7.8	7.4	0.42
	D10 cc	2.2	1.2	0.22
	V12 Gy	5.9	10.4	0.92
	V15 Gy	2.2	4.6	0.84
	V21 Gy	0	0	-

DX (the dose to X% of the Organ at Risks [OARs] volume) at X values of 0.1, 5.0, 10.0 cc.
VX (the percentage of the OARs volume that received more than X Gy)

Tab. 3. Treatment planned by medical physicist 2

		Empty	Full	p value
PTV	D0.1 cc	66	66	0.5
	D5 cc	56	53.4	0.29
	D10 cc	44	40.3	0.32
	V12 Gy	99.9	99.9	0.5
	V15 Gy	99.3	99.4	0.57
	V21 Gy	97.3	97.7	0.58
Stomach	D0.1 cc	19.8	20.3	0.32
	D5 cc	13.8	15.6	0.03
	D10 cc	12.3	14.3	0.02
	V12 Gy	7.7	6.9	0.36
	V15 Gy	2.5	2.2	0.37
	V21 Gy	0	0	-
Intestine	D0.1 cc	17.4	15.6	0.28
	D5 cc	13.1	11.1	0.23
	D10 cc	11.5	9.9	0.26
	V12 Gy	3.4	6.2	0.2
	V15 Gy	1.4	2.4	0.27
	V21 Gy	0	0	-
Pancreas	D0.1 cc	45.4	37.3	0.19
	D5 cc	25.8	19.1	0.16
	D10 cc	20	13.5	0.12
	V12 Gy	70.7	44.1	0.06
	V15 Gy	61.1	36.8	0.06
	V21 Gy	38.3	22	0.08
Liver	D0.1 cc	16.1	15.4	0.39
	D5 cc	12.6	11.9	0.38
	D10 cc	11.5	10.6	0.34
	V12 Gy	2.6	0.7	0.06
	V15 Gy	0.4	0.2	0.26
	V21 Gy	0	0	-
Left kidney	D0.1 cc	49.2	50.2	0.58
	D5 cc	32.1	29.6	0.3
	D10 cc	23.7	22	0.34
	V12 Gy	22.2	15.5	0.01
	V15 Gy	17.7	12.9	0.03
	V21 Gy	10.7	9	0.22
Right Kidney	D0.1 cc	10.7	11.3	0.61
	D5 cc	8.1	9	0.34
	D10 cc	6.9	8	0.3
	V12 Gy	2.6	2.3	0.55
	V15 Gy	0.5	1.5	0.26
	V21 Gy	0	0	-
Spinal cord	D0.1 cc	14.6	16.2	0.15
	D5 cc	7.8	6.9	0.3
	D10 cc	2.5	1.3	0.15
	V12 Gy	6.4	8.9	0.8
	V15 Gy	1.9	3	0.72
	V21 Gy	0	0	-

DX (the dose to X% of the Organ at Risks [OARs] volume) at X values of 0.1, 5.0, 10.0 cc. VX (the percentage of the OARs volume that received more than X Gy)

Blue line: adrenal CTV (2 mm margin from GTV), OAR: Liver (pink line), Stomach (purple line), Pancreas (yellow line), and Intestine (light blue line) (Figure 2).

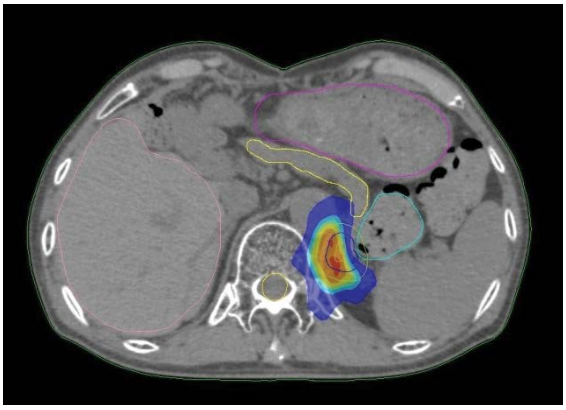

Fig.2. Adrenal SBRT in the setting of a large stomach

An example of adrenal SBRT in the setting of a small stomach. The pancreas is close to the left adrenal ground. CTV coverage is good. Light blue line: adrenal CTV (2 mm margin from GTV). OAR: Liver (pink line), Stomach (light orange line), Pancreas (light red line), and Intestine (blue line) (Figure 3).

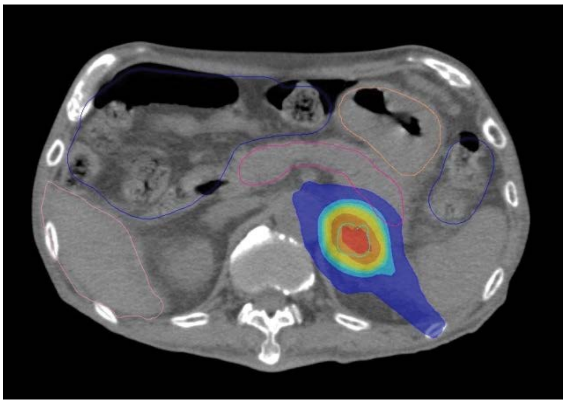

Fig.3. Adrenal SBRT in the setting of a small stomach

An example of adrenal SBRT in the setting of a small stomach. The left kidney is close to the left adrenal ground; however, left adrenal CTV coverage is good. Light blue line: adrenal CTV (2 mm margin from GTV). OAR: Liver (pink line), Stomach (light orange line), Pancreas (disappeared in this slide), and Intestine (disappeared in this slide)

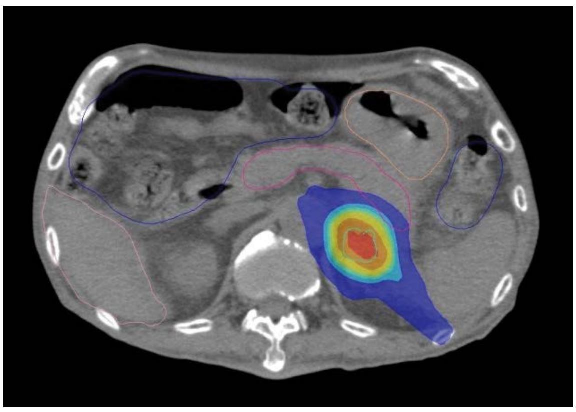

Fig.4. Adrenal SBRT in the setting of a small stomach

Colour dose wash list (Dose distribution of Figures 1-4). Prescribed dose is 54 Gy/6 fractions. When the area irradiated with 54 Gy is 100% (yellow), the percentage is expressed by colour.

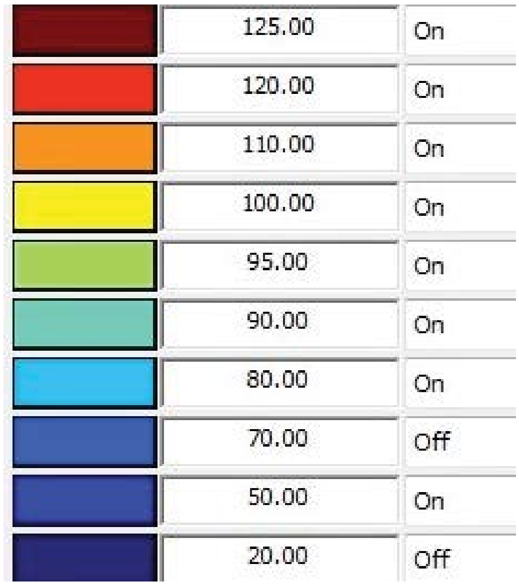

Fig.5. Dose distribution of Figures 1-4

All other organs (intestines, pancreas, liver, right kidney, and spinal cord) had equivocal OAR doses between the two groups (Figure 5).

DISCUSSION

According to previous reports [13,14], which is the most suitable balance between protecting the stomach and kidney? How Should I simulate a patient to assure the best dosimetrical outcome?

It was found that a smaller stomach was better separated from the left adrenal gland, and therefore received a smaller radiation dose. The pancreas is between the left adrenal gland and the stomach. Both the pancreas and the adrenal glands are retroperitoneal organs, but the stomach is not. In addition, although the image was taken in the supine position this time, it is possible that the distance between the stomach and the left adrenal gland can be further increased by positioning the patient in the left lateral decubitus or prone position.

In contrast to the stomach, the kidney is in contact with the adrenal gland as a retroperitoneal organ, and it is difficult to control its movement. However, it was observed that the larger the stomach, the lower the dose to the left kidney. The reason for this could be that the stomach squeezes the pancreas and the kidneys dorsally, causing the kidneys to move caudally and have a reduced radiation exposure. Moreover, it is important for patients with impaired renal function to increase gastric distension and move the left kidney caudally to reduce the dose to the kidney. In contrast, if the stomach has a lesion, the stomach and the adrenal glands may be separated from each other on an empty stomach. In addition, because the stomach on an empty stomach tends to maintain reproducibility [17], it may be possible to treat with the same accuracy as MR-liniac if the treatment is performed with high reproducibility on an empty stomach [15-16].

It has also been shown gastric volume varies significantly both between and within fractions (inter and intra-fraction motion) [13-16]. Because of close proximity of the stomach, patients with left-sided tumours were advised to fast for at least 2.5 h before simulation and treatment. Their results using MR-guided SBRT showed that, for left-sided adrenal tumours, the stomach V15 significantly decreased post-treatment; from a mean of 29.6 cc (5^{th}-95^{th} percentile range: 6.3 cc-72.4 cc) pre-treatment, to a post-treatment mean volume of 24.9 cc (3.9 cc-55.2 cc) ($p<0.0003$).

In addition, we thought it was necessary to irradiate the stomach with the same shape each time. As a method of making the shape of the stomach the same at each irradiation, compare whether it is better to make the stomach empty, or to did the patient drink about 400 ml of water each time before the treatment plan and irradiation to achieve reproducibility as a full stomach.

Control of bladder volume by drinking water is well known in IMRT for prostate cancer. However, it is done on the premise that the morphology of the bladder does not change so much as the capacity of the bladder increases. However, the stomach is a very moving organ.

Therefore, we thought that it would be difficult to match the shape by drinking water each time, and considered the empty stomach due to fasting as the control group. It was reported that the morphology of the stomach can be maintained by fasting the stomach. However, if the empty stomach causes an increase in the dose to the stomach, it is a complete fall, and this test was conducted.

It is difficult to reliably measure the small intestine because it is in a different position every day. In fact, even with a cone beam CT the position of the small intestine changes every time. It is true that drinking water when treating the stomach may change the dilation of the duodenum, but this degree of dilation varies from day to day, so it is difficult to control the small intestine.

The dose to the pancreas was not affected by stomach morphology. This is considered to be due to the close proximity of the left adrenal gland and the pancreas. However, the size of the pancreas also varies greatly for each patient, and visceral fat may easily adhere to the area around the pancreas, which may also be reduced by gaining weight.

CLINICAL PRACTICE

An empty and full stomach had an opposite effect on OAR to the stomach and left kidney during adrenal irradiation. Therefore, it is necessary to choose whether to prepare for this by reducing the dose to the stomach or reducing the dose to the left kidney. Findings here also suggest that it is useful to obtain treatment planning CTs with an empty and full stomach, permitting the creation of two SBRT plans.

In terms of choosing between SBRT with an empty or full, it is appropriate to decide this based on renal function and gastrointestinal condition (gastritis, etc.). Adrenal tumours are more likely to be metastatic deposits compared with primary tumours. Chemotherapy is often used for metastases, so it would be desirable to reduce the radiation dose to the kidneys in such cases.

It is also necessary to consider the positional relationship of organs, especially given differences in visceral fat between patients. The distance between the organ and the adrenal gland was not taken into consideration in this work, but it is expected that the more visceral fat, the greater the distance between the adrenal gland and the irradiated organ. If increasing the amount of visceral fat reduces the dose to OAR, temporarily gaining weight may be a solution to this issue.

LIMITATIONS

The following three issues can be considered for improvements in future works.

- SBRT to the right adrenal gland. Unlike the left adrenal gland, the right adrenal gland has less OAR but might involve an increased radiation dose to the inferior vena cava and biliary/bile duct pancreatic duct. Verification of this is required.
- Decrease the radiation dose to the target due to increased OAR restrictions as the dose increases. In general, the higher the dose, the higher the cure rate (SBRT to the lungs and liver in particular). Therefore, it is important to find a dose that can be traded off [6,7].
- It is desirable to place a gold marker in order to improve accuracy, but there is a risk of inserting it percutaneous. Because the adrenal gland is an organ that cannot be seen on X-ray, reproducibility is usually attempted by aligning it with the position of the vertebral body. However, it is also necessary to consider a method for narrowing the PTV margin by placing a gold marker.

FUTURE OUTLOOK (COMPARED WITH MR-LINAC)

It is expected that the number of indications for SBRT will continue to increase in the future. It is necessary to establish a plan to protect OAR by administering the minimum prescribed dose. Techniques for artificially moving the position of the OAR (sometimes PTV) to remove the heart from the irradiation field, such as respiratory synchronization that is used in breast conserving therapy in the management of left breast cancer will continue to be required. It is true that the shape of the body surface and the appearance of MR-Linac have made it possible to understand information on the body's surface and well within the abdomen.

This study reveals that the adrenal glands may be able to regulate the radiation dose to the stomach and left kidney by changing the shape (size) of the stomach. MRI-Linac can reduce the target's intra- and inter-variance but not the contents of the stomach [17]. Therefore, we believe that MR-Linac will become widespread, but also that such a method of artificially changing the shape and position of organs is necessary.

Therefore, if the organ position can be controlled by some kind of pre-treatment, it is worth attempting.

CONCLUSION

When SBRT was performed on the left adrenal gland, it was found that the smaller the stomach size, the lower the dose to the stomach. The stomach is an abdominal organ that can be artificially resized. Therefore, it is better to perform SBRT on patients with an empty stomach. Furthermore, because it is easy for the empty stomach to have the same stomach shape every time due to fasting, it is better to plan SBRT on an empty stomach than to plan with the full stomach.

CONFLICT OF INTEREST

There are no conflicts of interest to report.

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